

AMENDMENTS TO THE SPECIFICATION

1. Please replace paragraph 7 (lines 29-35) on page 2 with the following paragraph:

--It proves that amino acids 70-74 in HLA-DR β 1 contain a consensus sequence of QK[[/R]]RAA (SEQ ID NO:9) or QRRAA (SEQ ID NO:10) (i.e. Gln-Lys/Arg-Arg-Ala-Ala, glutamine-lysine/arginine-arginine-alanine-alanine)⁽¹⁾. This consensus sequence is related to the formation of HLA-DR β 1-antigen binding cleft and is the functional amino acids which function in the binding to antigens. Plenty of research by the inventors and Wucherfennig *et al.* proved that positively charged amino acid 71 (Lys or Arg) in this sequences is the key site of antigen binding⁽²⁻⁸⁾--

2. Please replace Table 1 (lines 11-20) on page 3 with the following table:

--Table 1. Amino acids binding to T cell receptors and HLA- DR β 1 in CII

DR β 1	(<u>SEQ ID NO:8</u>)							
↑	↑	↑	↑	↑	↑	↑	↑	
F	K	G	E	Q	G	P	K	
263	264	265	266	267	268	269	270	
				↓	↓	↓	↓	
				TCR	TCR	TCR	TCR	

* F = Phe (Phenylalanine), K = Lys (Lysine), G = Gly (Glycine), E = Glu (Glutamate), Q = Gln (Glutamine), P = Pro (Proline), [[A]] R = Arg (Arginine), A = Ala (Alanine)--

3. Please replace paragraph 3 (lines 31-40) on page 3 with the following paragraph:

--Therefore, in the embodiments of the present invention, non-T cell binding peptides and their analogs are provided. The following peptides are preferred: FKGEAGPKGE (SEQ ID NO:1), FKGEQAPKGE (SEQ ID NO:2), FKGEQGAKGE (SEQ ID NO:3), FKGEQGPAGE (SEQ ID NO:4), FKGEQGAAGE (SEQ ID NO:5), FKGEQAGAGE (SEQ ID NO:6), and FKGEGAGAGE (SEQ ID NO:7). These polypeptides can bind to the specific sequence of QK[[/R]]RAA (SEQ ID NO:9) or QRRAA (SEQ ID NO:10) (i.e. Gln-Lys/Arg-Arg-Ala-Ala) in HLA- DR β 1 which is related to the onset of rheumatoid arthritis, and can thereby inhibit T cell activation, and consequently reach

the goal of treating rheumatoid arthritis and other autoimmune diseases mediated by T cells.--

4. Please replace Table 6 (lines 1-5) on page 6 with the following table:

--Table 2. Design of non-T cell binding peptides

Names of polypeptides	Amino acid position									
	263	264	265	266	267	268	269	270	271	272
CII WTM <u>(SEQ ID NO:8)</u>	F	K	G	E	Q	G	P	K	G	E
267A <u>(SEQ ID NO:1)</u>	-	-	-	-	A	-	-	-	-	-
268A <u>(SEQ ID NO:2)</u>	-	-	-	-	-	A	-	-	-	-
269A <u>(SEQ ID NO:3)</u>	-	-	-	-	-	-	A	-	-	-
270A <u>(SEQ ID NO:4)</u>	-	-	-	-	-	-	-	A	-	-
Mut 269-270 <u>(SEQ ID NO:5)</u>	-	-	-	-	-	-	A	A	-	-
Mut 268-270 <u>(SEQ ID NO:6)</u>	-	-	-	-	-	A	G	A	-	-
Mut 267-270 <u>(SEQ ID NO:7)</u>	-	-	-	-	G	A	G	A	-	-

5. Please replace paragraph 8 (page 2, line 36 to page 3, line 40) with the following paragraph:

--By research on crystal structure of HLA-DR β 1-antigen dim[[m]]er using X-ray diffraction technique, it is found that a variety of antigen peptides which bind to rheumatoid arthritis related to HLA-DR β 1 (DR4/DR1) molecules are extremely similar in configuration, including denatured type II collagen (CII) and Heat Shock Protein (HSP)⁽⁹⁻¹²⁾. From the tridimensional 3-dimentional structures of these peptides (Figure 1), it can be seen that the side chains of Phe263 (P1), Glu 266 (P4) and Gly271 (P9) stretch to the HLA- DR β 1 molecule in the left, and are imbedded into the antigen binding cleft entirely or partially, while side chains of the other amino acids stretch to another side of the side opposite to HLA- DR β 1 (the side of T cell receptor) to stimulate T cell activation. From figure 2, it can be seen that the side chains of P1, P4, and P9 of CII polypeptide are imbedded into the antigen binding "pocket" of HLA- DR β 1. Negatively charged P4 (Glu) is adjacent to positively charged amino acid 71 (Lys71) of HLA- DR β 1, which forms the polar binding

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with high affinity. Therefore, Glu 263, Gly265, Gly 266, Gly 271, and Glu 272 and thus activates T cells. From this we can see that the major HLA- DR β 1 binding amino acids in CII polypeptide are Phe 262, Gly265, Gly266, Gly 271, and Glu 272, whilst the major T cell receptor (TCR) binding amino acids are Gln 267, Gly 268, Pro 269 and Lys 270 (Table 1).--